

Local stability analysis of an influenza virus transmission model case study: tondano health center in pekalongan city

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Local stability analysis of an influenza virus transmission model case study: tondano health center in pekalongan city

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Abstract. Influenza Virus is an infectious disease caused by the *Orthomyxoviridae* virus. This paper discussed mathematical modeling that explains the model of the influenza virus transmission with SEIR model, where S is susceptible, E is exposed, I is infected, and R is recovered. Basic reproduction numbers (R_0) are used to analyze the stability of the model.

When R_0 less than 1 the virus free equilibrium is stable asymptotically local, while when R_0 greater than 1 the endemic equilibrium is stable asymptotically local. From the numerical simulation results based on data from Pekalongan, Indonesia, it's found that reproduction number is equal to 0,03492209390. This indicates that the virus free equilibrium is locally asymptotically stable and the endemic equilibrium is not locally asymptotically stable, so that there is no virus transmission in Pekalongan.

1. Introduction

Influenza or commonly known as flu is a disease caused by the *Orthomyxoviridae* virus where the virus attacks the nose, throat, bronchi, and sometimes the lungs. Common symptoms of influenza in humans are fever with a temperature above 38° Celsius, coughing, headache, snuffle, and an uncomfortable body called ILI or Influenza Like Illness [1]. The duration of virus transmission is between 2-7 days and usually can be healed by itself [2]. Indonesia people also called this flu as a self limiting disease [3]. If there are no complications with other diseases, then after 4-7 days the disease will gone. A person's immune system will greatly affect the severity of the disease [4]. Respiratory transmission depends on the production of airborne particles and aerosols that contain viruses. Aerosols are produced during normal speech and breathing. Expulsion from the nasal cavity by sneezing and will be more effective if the infection produces more snot [5].

The transmission of the influenza virus can be studied with mathematical modeling. Mathematical models have provided useful tools for understanding the dynamics of an influenza virus transmission. Mathematical models that discuss the transmission of disease or epidemic models are the right method to study the pattern of an influenza virus transmission to humans [6-9]. Nguyen Huu Khanh considers the SEIR model that describes the transmission of the influenza virus by paying attention to the disease resistance in humans. So that in the model, a person in exposed individual or infected individual can go back to susceptible individual without treatment [10]. This model is constructed by a system with four differential equations depending on the parameters. By using the Next Generation



Matrix method, a threshold of R_0 is called the basic reproduction number. In general, when $R_0 < 1$ the virus will dies out, and when $R_0 > 1$ the virus still exists in the population [11].

2. Mathematical Modelling of an Influenza Virus Transmission

In this model the SEIR model is used in which the total human population (N) is divided into four subpopulations. $S(t)$ is the number of susceptible individuals at the time, $E(t)$ is the number of exposed individuals at the time, $I(t)$ is the number of infected individuals at the time, and $R(t)$ is the number of recovered individuals at the time. Nguyen Huu Khanh considers the SEIR model that describes the transmission of the influenza virus by paying attention to the disease resistance in humans. So that in the model, a person in exposed individuals or infected individuals can go back to susceptible individuals without treatment [10].

The parameters that used in the influenza virus transmission model are: Λ is constant recruitment of susceptible human, γ is contact rate of virus transmission, c is rate at which the exposed human become to be susceptible human without treatment, b is rate at which the infected human become to be susceptible human without treatment, ε is rate at the exposed human that shows symptoms of infection, α is rate at which the recovered human become to be susceptible human again, β is rate at which the infectious human become to be the recovered human, and μ is rate at natural death.

We assume that the total size of the population $N(t)$ is constant, that is $N(t) = N$. Then $\bar{S}(t) + \bar{E}(t) + \bar{I}(t) + \bar{R}(t) = N$. Let $S(t) = \frac{\bar{S}(t)}{N}$, $E(t) = \frac{\bar{E}(t)}{N}$, $I(t) = \frac{\bar{I}(t)}{N}$, $R(t) = \frac{\bar{R}(t)}{N}$. we obtain the reduced system are

$$\begin{aligned} \frac{dS}{dt} &= \mu - \gamma S(E + I) + cE + bI + \alpha R - \mu S, \\ \frac{dE}{dt} &= \gamma S(E + I) - (c + \varepsilon + \mu)E, \\ \frac{dI}{dt} &= \varepsilon E - (\beta + b + \mu)I, \\ \frac{dR}{dt} &= \beta I - (\alpha + \mu)R, \end{aligned} \quad (1)$$

with the condition $S(t) + E(t) + I(t) + R(t) = 1$.

Then from the model, we find the equilibria. To find the equilibria we set the right-hand side of the system (1) equals zero. Based on the system of differential equations (1) two equilibria are obtained:

Virus free equilibrium is the point where a population is free of viruses, so that there is no individual has been infected with the influenza virus ($E_0 = 0$, and $I_0 = 0$). We got the virus free equilibrium is $P_0 = (S_0, E_0, I_0, R_0) = (1, 0, 0, 0)$. It is seen that the equilibrium P_0 always exists.

Endemic equilibrium is a condition where in a equilibrium there is at least one infected individual and then infects or transmits to another individual.

The endemic equilibrium are:

$$P_1 = (S_1, E_1, I_1, R_1) = \left(\frac{1}{R_0}, \frac{(\alpha + \mu)(\beta + b + \mu)G_1}{G_2}, \frac{\varepsilon(\alpha + \mu)G_1}{G_2}, \frac{\beta\varepsilon G_1}{G_2} \right),$$

$$\text{where } R_0 = \frac{\gamma(\beta + b + \mu + \varepsilon)}{(c + \varepsilon + \mu)(\beta + b + \mu)},$$

$$G_1 = ((\beta + b + \varepsilon + \mu)\gamma - (\beta + b + \mu)(c + \varepsilon + \mu)), \text{ and}$$

$$G_2 = \gamma(\beta + b + \varepsilon + \mu)(\beta\varepsilon + (\alpha + \mu)(\beta + b + \varepsilon + \mu)).$$

When $R_0 > 1$, we have $G_1 > 0$. This implies the equilibrium P_1 exists as $R_0 > 1$.

Then be given the value of the basic reproduction number (R_0). Basic reproduction numbers are the parameters that used to determine the extent of influenza virus transmission in the human population. (R_0) is obtained by determining the largest eigenvalue of the Next Generation Matrix, so we have

$$R_0 = \frac{\gamma(\beta + b + \mu + \varepsilon)}{(c + \varepsilon + \mu)(\beta + b + \mu)},$$

when $R_0 < 1$ the virus will dies out, and when $R_0 > 1$ the virus still exists in the population [11].

3. Local Stability Analysis

Stability Analysis of Virus Free Equilibrium can be analyzed the stability with the first-order Taylor linearization from the system of nonlinear equations (1). Obtained by the Jacobian matrix at the virus free equilibrium that has been linearized as follows,

$$J(P_0) = \begin{bmatrix} -\mu & -\gamma + c & -\gamma + b & \alpha \\ 0 & \gamma - (c + \varepsilon + \mu) & \gamma & 0 \\ 0 & \varepsilon & -(\beta + b + \mu) & 0 \\ 0 & 0 & \beta & -(\alpha + \mu) \end{bmatrix},$$

so the we find the eigen values from the jacobian matrix at the virus free equilibrium are as follows

$$\lambda_1 = -\mu,$$

$$\lambda_2 = -(\alpha + \mu),$$

$$\lambda_3 = -\frac{1}{2}(L + \sqrt{L^2 + 4G_1}),$$

$$\lambda_4 = -\frac{1}{2}(L - \sqrt{L^2 + 4G_1}),$$

with

$$L = \beta + b + c + \varepsilon + 2\mu - \gamma,$$

and

$$G_1 = (\beta + b + \varepsilon + \mu)\gamma - (\beta + b + \mu)(c + \varepsilon + \mu).$$

Theorem 3.1 [4]. Virus Free Equilibrium $P_0 = (S_0, E_0, I_0, R_0)$ will be locally asymptotically stable when $R_0 < 1$ otherwise when $R_0 > 1$ the Virus Free Equilibrium $P_0 = (S_0, E_0, I_0, R_0)$ will not locally asymptotically stable.

Proof

Proven $P_0 = (S_0, E_0, I_0, R_0)$ locally asymptotically stable. Based on the above theorem, it is shown that all eigenvalues of the Jacobian matrix are negative. The eigenvalues of the Jacobian matrix are obtained from equation (1) as follows

$\lambda_1 = -\mu$, because the value of μ is always positive then the eigenvalue $\lambda_1 < 0$.

$\lambda_2 = -(\alpha + \mu)$, because the value of α and μ is always positive then the eigenvalue $\lambda_2 < 0$.

$\lambda_3 = -\frac{1}{2}(L + \sqrt{L^2 + 4G_1})$, the value of L and G_1 is always positive then the eigenvalue $\lambda_3 < 0$.

$\lambda_4 = -\frac{1}{2}(L - \sqrt{L^2 + 4G_1})$, then will be proven $\lambda_4 < 0$, based on $R_0 < 1$, proven that $\lambda_4 < 0$. So

that the free virus equilibrium $P_0 = (S_0, E_0, I_0, R_0)$ are locally asymptotically stable when $R_0 < 1$ it means that the virus does not spread to other individuals and in the end the virus will disappear from the population. Otherwise when $R_0 > 1$ so the free virus equilibrium $P_0 = (S_0, E_0, I_0, R_0)$ will not locally asymptotically stable, it means the virus is still in the population and will infect other individuals. Why did I prefer to choose local stability analysis than global stability analysis is because to analyze global stability analysis would make bachelor quite complicated in completing the analysis, so I chose the local stability analysis to make it easier. Which one is the better result? Local or Global? I don't know yet because my research is limited to local stability analysis.

Analysis of Endemic Equilibrium. Based on the analysis of the mathematical model at the endemic equilibrium, the Jacobian matrix is obtained as follows

$$J(P_1) = \begin{bmatrix} -W(\beta + b + \mu + \varepsilon) - \mu & -(K - c) & -(K - b) & \alpha \\ W(\beta + b + \mu + \varepsilon) & (K - c - \varepsilon - \mu) & K & 0 \\ 0 & \varepsilon & -(\beta + b + \mu) & 0 \\ 0 & 0 & \beta & -(\alpha + \mu) \end{bmatrix}, \quad (2)$$

with $W = \frac{\gamma(\alpha + \mu)G_1}{G_2}$, and $K = \frac{\gamma}{R_0}$.

The characteristic equation of the Jacobian matrix $J(P_1)$ is in the form of polynomials, as follows

$$\lambda^4 + a_3\lambda^3 + a_2\lambda^2 + a_1\lambda + a_0 = 0,$$

with

$$a_4 = 1,$$

$$a_3 = (\alpha + \beta + b + c + \varepsilon + 2\mu - \gamma) + 2\mu + \gamma(G_2 + (\alpha + \mu)(L_1 + \varepsilon)) \frac{G_1}{G_2},$$

$$a_2 = \mu(L_1 + L_2) + (\alpha + \mu + L_1)(\mu + L_2 + \gamma(E_1 + I_1 - S_1)),$$

$$a_1 = (\alpha + \mu)\gamma(L_1 + \varepsilon)^2 ((\beta + \mu)\varepsilon + (\alpha + 2\mu)L_1 + (\alpha + \mu)(\varepsilon + \mu)) \frac{G_1}{G_2} + (\alpha + \mu)\mu(\mu L_1 + \varepsilon L_2),$$

$$a_0 = \gamma(E_1 + I_1)(\varepsilon\mu(\alpha + b + \mu) + \alpha(\alpha + \mu)L_1),$$

According to the Routh Hurwitz stability criteria, the endemic equilibrium $P_1 = (S_1, E_1, I_1, R_1)$ will be asymptotically stable if

$$a_0 > 0, a_1 > 0, a_2 > 0, a_3 > 0, a_4 > 0, a_2a_3 - a_1 > 0, \text{ and } a_1(a_2a_3 - a_1) - a_0a_3^2 > 0.$$

4. Numerical Simulation

In this discussion a model simulation was given to determine the transmission of influenza virus with disease resistance in the Tondano Health Center in East Pekalongan Subdistrict, Pekalongan City. Why did i take a case study in Pekalongan city is because the data of influenza disease in Pekalongan city is exists while in other cities like Semarang there are none. Why the city of Semarang has no data on influenza disease because they only focus on major diseases. So this is my reason why did i take a case study in Pekalongan city, especially on Tondano Health Center.

We have a model for the transmission of influenza viruses with the disease resistance as follows:

$$\frac{dS}{dt} = 0,0003 - 0,008S(E + I) + 0,076E + 0,9I + 0,02R - 0,0003S,$$

$$\frac{dE}{dt} = 0,008S(E + I) - (0,076 + 0,2 + 0,0003)E = 0,008S(E + I) - 0,276E,$$

$$\frac{dI}{dt} = 0,2E - (0,07 + 0,9 + 0,0003)I = 0,2E - 0,97I,$$

$$\frac{dR}{dt} = 0,07I - (0,02 + 0,0003)R = 0,07I - 0,0203R,$$

with initial values $S(0) = 1658$ individual/month, $E(0) = 1808$ individual/month,

$I(0) = 153$ individual/month, $R(0) = 131$ individual/month.

The solution models that obtained by calculations using maple program as follows

1. Virus Free Equilibrium

From the calculation we got the virus free equilibrium $P_0 = (S_0, E_0, I_0, R_0) = (1, 0, 0, 0)$.

We obtained the Jacobian matrix from the virus free equilibrium are as follows

$$J(P_0) = \begin{bmatrix} -0,0003 & 0,0068 & 0,892 & 0,02 \\ 0 & -0,2683 & 0,008 & 0 \\ 0 & 0,2 & -0,9703 & 0 \\ 0 & 0 & 0,07 & -0,0203 \end{bmatrix}.$$

The Jacobian matrix eigenvalue of the virus-free equilibrium point is -0.0003; -0.0203; -0.266028; -0.972571. Because all eigenvalues of the Jacobian matrix are negative so that the model is stable asymptotically local in free virus equilibrium point which means that there is no influenza virus transmission in the population at the District of East Pekalongan.

2. Endemic Equilibrium

From the calculation we got the endemic equilibrium P_1 as follows:

$$P_1 = (S_1, E_1, I_1, R_1)$$

$$P_1 = \left(\frac{1}{R_0}, \frac{(\alpha + \mu)(\beta + b + \mu)G_1}{G_2}, \frac{\varepsilon(\alpha + \mu)G_1}{G_2}, \frac{\beta\varepsilon G_1}{G_2} \right)$$

$$P_1 = (28.635167, -14.416693, -2.9715949, -10.246879).$$

To test the stability of the system we have two ways, there are:

i. Find the Eigenvalues from the Jacobian Matrix

By substituting the parameter values in the system of differential equations (2) is obtained by the Jacobian matrix from the endemic equilibrium as follows

$$J(P_1) = \begin{bmatrix} 0,138806 & -0,153081 & 0,670918 & 0,02 \\ -0,139106 & -0,047218 & 0,22081 & 0 \\ 0 & 0,2 & -0,9703 & 0 \\ 0 & 0 & 0,07 & -0,0203 \end{bmatrix}.$$

The eigenvalue from Jacobian matrix of the endemic equilibrium point is 0.165903; -0.0003; -0.030617; -1.033997. Because there is a positive eigenvalue from Jacobian matrix so that the model is not locally asymptotically stable in endemic equilibrium, which means that there is no influenza virus transmission in the population.

ii. Routh-Hurwitz

Order conditions that the Routh-Hurwitz criteria can be fulfilled, are

$$a_0 > 0, a_1 > 0, a_2 > 0, a_3 > 0, a_4 > 0, a_2 a_3 - a_1 > 0, \text{ dan } a_1 (a_2 a_3 - a_1) - a_0 (a_3)^2 > 0.$$

Based on Maple's calculation, the values of the coefficients are as follows:

$$a_0 = -0.00006248, a_1 = -0.00620451, a_2 = -0.09035273, a_3 = 1.11802384, a_4 = 1,$$

$$a_2 a_3 - a_1 = -0.09481199, a_1 (a_2 a_3 - a_1) - a_0 (a_3)^2 = 0.0006663.$$

Based on the above calculation, it was found that the Routh-Hurwitz criteria were not fulfilled, that is

$$a_0 < 0, a_1 < 0, a_2 < 0, a_2 a_3 - a_1 < 0, \text{ dan } a_1 (a_2 a_3 - a_1) - a_0 (a_3)^2 < 0.$$

It means that the model of influenza virus transmission is not locally asymptotically stable in endemic equilibrium point which means that there is no influenza virus transmission in the population.

The following is a graphical picture of an influenza virus transmission model in each sub-population with initial values $S(0) = 1658$ individual/month, $E(0) = 1808$ individual/month, $I(0) = 153$ individual/month, $R(0) = 131$ individual/month.

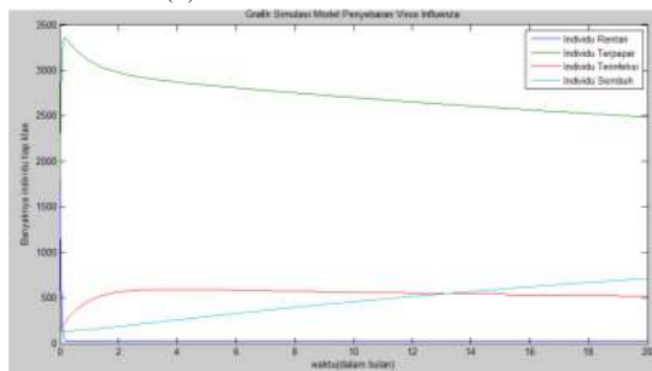


Figure 4.1. Graph of the Influenza Virus Transmission Model Simulation

Figure 4.1 shows the change of the number in each sub-populations of susceptible individuals, exposed individuals, infected individuals, and recovered individuals, from $t = 0$ to $t = 20$ month.

At first, susceptible individuals in East Pekalongan subdistrict were 1658 people. The number of proportions of individuals susceptible are decreases but after that it changes in to constant or equal, this is because there were the entry of individuals exposed, infected, and recovered who become susceptible individuals again without treatment.

Furthermore, the proportion of individuals who were exposed was 1808 people. The proportion of individuals exposed are increased but after reaching its peak, the proportion of individuals exposed

gradually decreases. This is because there is a good disease resistance in individuals exposed so that they are not infected with influenza virus.

As for the proportion of infected individuals are 153 people, and from the graph could be seen that infected individuals have increased. But after reaching its peak, the proportion of infected individuals gradually decreased.

The proportion of individuals who recovered are 131 people, and from the graph could be seen that when the proportion of infected individuals slowly decreased, the proportion of recovered individuals is significantly increased.

Based on equation (3), the basic reproduction number of the above parameters is 0.03492209390 ($R_0 < 1$), which means that there is no transmission of the influenza virus in the population. Based on the stability analysis that has been carried out, we obtained the virus free equilibrium is locally asymptotically stable.

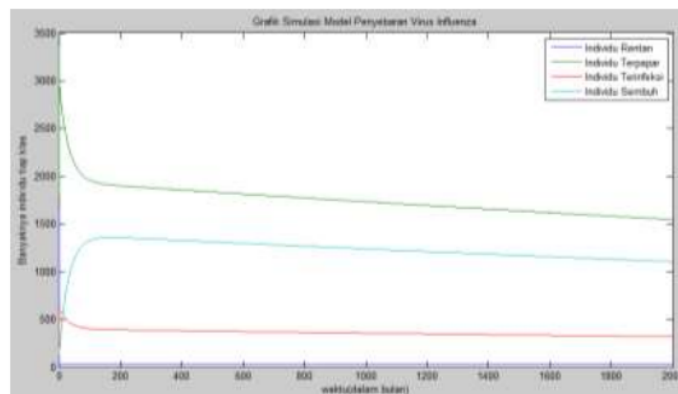


Figure 4.2. Graph Simulation of Influenza Virus Transmission Model

Figure 4.2 shows the change of the number in each sub-populations of susceptible individuals, exposed individual, infected individuals, and recovered individuals, from $t = 0$ to $t = 2000$ month. When we take $t = \infty$, so we have a graph that all the numbers of individuals from each sub-population will lead to a virus free equilibrium $P_0 = (1,0,0,0)$.

5. Conclusions

This paper is studied the mathematical model of an influenza virus transmission with disease resistance. The discussion that has been carried out in this mathematical model is obtained by two equilibria, the virus free equilibrium and the endemic equilibrium. Stability analysis at the virus free equilibrium P_0 is stable if $R_0 < 1$, and will be stable at the endemic equilibrium P_1 if $R_0 > 1$.

Based on the simulation using data from Tondano Health Center in Pekalongan City in 2017, the basic reproduction number of influenza virus is 0.03492209390 ($R_0 < 1$), and because all eigenvalues of the Jacobian matrix are negative, the virus free equilibrium is stable. This indicates that there is no transmission of the influenza virus in the human population in Tondano Subdistrict, Pekalongan City.

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